BONE REGENERATION IN NOVEL

POROUS TITANIUM IMPLANTS

by

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INTRODUCTION

Dental implants have mainly three types of macro-retentive features: screw threads (tapped or self tapping), solid body press-fit designs and/or porous-coated technologies. While the threaded design is currently by far the most popular one clinically, porous-coated press-fit implants have also been successful in certain clinical applications. Many clinical studies performed on the commercial porous-coated press-fit implant system (Endopore) show high success when used as short implants.[1, 2] They have been successfully used as abutments for over dentures,[1, 3-5] replacing missing teeth especially in narrow areas,[6-10] and in areas of maxillary sinus proximity and low levels of bone.[4, 8, 11-14] The coating technique was first developed for orthopedic prostheses like femoral stems by using different sintering techniques to form a mesh or a sintered bead surface for bone to grow into.[1, 2-4] In the 1980s, Pilliar and group[1, 2, 4] examined the use of these implants in endosseous designs. Several studies were carried out and results showed 93 percent to 100 percent relative success in three to five years with very short implants (7.7 mm) even in the posterior maxilla, which led to the development of the implant system (Endopore, Innova Corp., Toronto, Canada).[1,2, 4] Initial healing periods are shorter than for the traditional screw type: 10 weeks for the anterior mandible; and 16 weeks for the maxilla and posterior mandible. Clinical studies have suggested that when Endopore implants are placed in acceptable bone quality they would be able to function in a period shorter than that of longer length implant designs.[1, 4] The porous surface helps in bone contact, and is formed by sintering which is a diffusion process that bonds the titanium Ti-6Al-4V particles 44 to 150 μm in size to each other and to the titanium

substrate surface using high temperature and controlled atmosphere. It includes a solid-state diffusion that leads to particle-particle and particle substrate junctions to make and maintain interconnected openings all over the sintered surface. Endopore has a multilayered surface with pores ranging from 50 μm to 200 μm, 35 volume-percent porosity, a range in thickness of the porous area of around 0.3 mm, and a surface area that ranges between 512 mm to 638 mm, which is the highest surface area/unit implant length of the implant systems and which allows for faster bone formation during initial healing than threaded implants.[1, 3]

On the other hand, rapid manufacturing (RM) [1] is a novel processing method developed in the last two decades. It uses a computer-controlled heating source to create three-dimensional (3D) objects from metal powders to replicate the 3D profile from a Computer-Aided-Design (CAD) program or patient's computer tomography (CT) data. RM decreases lead-time and increases the build flexibility for low volume production of customized metal parts. Depending on the manufacturing method, several RM machines are available, including selective laser sintering (SLS), laser micro sintering, selective laser melting (SLM), three- dimensional (3-D) laser cladding, electron beam sintering (EBS) and electron beam melting (EBM).[14] Electron Beam Melting (EBM) has been used to make porous Ti-6Al-4V titanium structures for orthopedic applications.[15] The manufacturing process controls the problems of high chemical affinity of liquid titanium with atmospheric gases, which decreases ductility of the metal. To investigate the *in vivo* performance of these implants, a study was done using a smooth compact and porous Ti-6Al-4V device made by the EBM technique as scaffolds for bone formation. It shows that highly porous titanium implants made using EBM are appropriate scaffolds for bone

in growth.[16] Fifteen pigs with skull defects were used and EBM implants were placed in those defects. Microradiographs and histomorphometric analyses performed at 14 days, 30 days, and 60 days after surgery showed bone ingrowths increased to 14 percent, 30 percent and 46 percent, respectively. EBM has also been used to make personalized dental implants with a porous surface that provides better osseointegration.[16] The root form and the abutment are made as one piece and have the same shape of the patients tooth. Scanning a tooth by computer tomography does it and then it is converted to a computer-aided design to be produced by EBM (Figure 1). This may reduce surgery and recovery times and could be more cost effective. In mechanical properties, EBM samples have ultimate tensile strength of 1,028 MPa and 14 percent in tensile strain, similar to the mechanical properties of wrought Ti-6Al-4V.[17] Since the EBM specimens will be made by Ti-6Al-4V, we also do not expect problem in its biocompatibility. However, there has been very limited information about the *in vivo* performance of these implants. Moreover, the *in vivo* performance of EBM implants has never been evaluated side-by-side with commercially-available porous-coated press-fit implants.

PURPOSE OF THE STUDY

The objective of this study was to evaluate the *in vivo* performance of the novel dental implant fabricated via the rapid-prototyping technique, electron beam melting (EBM), and compare it to the commercially-available porous-coated press-fit dental implants (Endopore, Innova Corp.). This study is important as a preliminary study to examine the bone to implant integration of EBM and the potential application of EBM. We plan to use a drilling method to standardize the size of osteotomy to evaluate the osteointegration of the implants. We do recognize that the future implant site may be an

extraction socket, which will have a different bone healing physiology compared to a drilled hole. However, we think the standardization is important in this preliminary study. Moreover, it is possible that in the future the extraction sockets may also be perforated to increase blood flow and to facilitate bone regeneration, which bear some similarities to the healing environment seen by drilling.

NULL HYPOTHESIS

There is no difference in bone to implant contact and pushout strength between EBM implants and the Endopore commercial dental implants after being implanted in rabbit tibia for six weeks.

ALTERNATIVE HYPOTHESIS

There is a statistically-significant difference in the bone-to-implant contact and pushout strength between the EBM implants and the Endopore commercial dental implants after being implanted in rabbit tibia for six weeks.

REVIEW OF LITERATURE

Dental implants have the ability of restoring the patient's teeth contour, esthetics, speech and health, which are the main goals of modern dentistry. The main function of a dental implant is to act as an abutment for a prosthetic device, and provide the same functions as of a natural tooth.[18] The number of implants used in the United States has increased from 1983 until the present by about more than tenfold. More than 90 percent of dentists offer dental implant treatment to their patients, and more than one million implants are inserted each year.[19]

The increased need for dental implants results from the aging population living longer, tooth loss related to age consequences of prosthetic failure, anatomic consequences of edentulism, poor performance of removable prosthesis, psychological aspects of tooth loss, advantages that implant supported restorations provide, predictable long term results of implant prosthesis, and increased public awareness.[19]

After many years of experimenting in bone, P.I. Brånemark[20] found the phenomenon of osseointegration in the early 1950s. It was first described as a histological condition where direct bone-to-implant contact could be seen under the light microscope.[20] This definition could not be applied clinically, so another definition by Zarb and Albrektsson[21] introduced "a process whereby clinically asymptomatic rigid fixation of alloplastic materials is achieved and maintained in bone during functional loading." Rigid fixation is a clinical term for implants, which describes the absence of observed clinical mobility with vertical or horizontal forces under 500 g. For years, rigid fixation and osseointegration have been used interchangeably. Today, "lack of mobility"

is used in implant movement, and is a clinical condition most often used to indicate implant integration.[21]

A range of dental implants were tested clinically and *in vitro* for about 30 years before they received worldwide acceptance.[22]

Since the very early designs of the 1960s, endosseous "endosteal and intraosseos" dental implants have been constantly modernized and adjusted and became more accepted with the introduction of the single root tooth by Brånemark.[2] The high success of endosseouss implants is due to the initial stability of the implant and the amount, quality and distribution of bone within the implant site.[23] In a meta-analysis, Lindh et al.,[24] stated that the success of implants placed in the posterior maxilla was less than other regions of the mouth and depends on the amount of bone in the area. The response of trabecular bone to the mechanical environment is a vital factor, especially in areas where the cortical thickness of bone and local material properties are inadequate to resist vertical forces.[24] The long-term success of implants does not only depend on bone stability, but transmucosal implants or the implant abutment interface also plays an important role in implant success.[23] To facilitate the improvement of implant therapy, lots of work has been done in developing implant biomaterials. These technologies have grown and improved from changing the surface oxides to nano-scale technologies.[23]

Implants used in the oral cavity have one of three major types of macro-retentive features: screw threads (tapped or self tapping), solid body press-fit designs and/or sintered bead technologies. The threaded design has lasted for a long time, but cylindrical implants without threads, showed preliminary osseointegration, and led to high secondary loss of bony support. They are designed to allow initial implant stability

and to create large spaces to allow bone growth. Bone has the ability to favorably respond to compressive loads (without the presence of a PDL) but not to shear forces. Hence, screw thread designs have been adapted to achieve a compressive loading of the surrounding bone.[23]

THE ENDOPORE DENTAL IMPLANT SYSTEM

In the late 1960s, porous surface implants for bone interfacing purposes were found by the University of Toronto. Orthopedic prosthesis like femoral stems, pelvic acetabular caps, etc. have used different sintering techniques to form a mesh or sintered beads as a surface for bone to grow into.[1, 4] In the 1980s, Pillar and group[1, 4] started research supported by the Medical Research Council of Canada to examine the use of these porous implants in endosseuos designs. Lots of successful studies have been done and results show a 93 percent to 100 percent relative success in 3 to 5 years with very short implants (7.7 mm) even in the posterior maxilla, which lead to the development of the implant system (Endopore). Clinical trials began at the University of Toronto in 1989.[1, 4]

The design of the Endopore implant is unique in various ways, it is truncated, conical, and tapered in shape, which helps to seat it in and allows for a lasting more durable implant. It also insures a firm fit to bone; moreover it allows a more contained surgical procedure, by less removal of bone in the apical portion and decreasing the potential of injury of the adjacent teeth and bone. Initial healing periods are shorter than the traditional screw type: 10 weeks for the anterior mandible and 16 weeks for the maxilla and posterior mandible. Clinical studies have reflected that when the Endopore implants were placed in acceptable bone quality they were able to function within 10

weeks, or a period shorter than that of longer length implant designs.[1, 4] The Endopore implants are present in a variety of lengths, widths and diameters. The greatest diameter (5 mm wide body) implants are used for posterior mandibular and maxillary regions, that need those types due to the bone condition and quality[1, 4, 6] They are available in shorter implant lengths 7.0 mm, 9.0 mm, and 12 mm. The 3.5 mm mini implant is used for the anterior part of the maxilla and mandible in which a narrower sized implant is required for small spaces. The most frequently used Endopore implants are the ones that are 4.1 mm in diameter and are 7 mm, 9 mm, and 12 mm in length. Endopore has made a high achievement when using relevantly shorter implant lengths than other designs. They can be easily used in areas that have a crown-to-root ratio lower than that normally recommended for other implant types, normal teeth, and when the apical cortical bone does not need to be engaged by the implant. One of the reasons for introducing roughened surfaces was to see if the change in the surface of the implants would improve their performance in short lengths. Sintered porous-surfaced (SPS) press-fit implants perform well in lengths of 7 mm[12-14] because of the three-dimensional interlock by bone ingrowths into their macro porous surface layer, transferring the stress to bone under loading. Measurement of SPS implant stability using an electronic mobility testing machine from baseline (1 month after prosthesis insertion) to 2 years in function showed that 7-mm-long, 4.1-mm-diameter SPS implants were as stable as the ones with the same diameter but with longer lengths (9 mm or 12 mm). In addition, as the time in function increased, SPS implants became more stable, leading to continued bone growth and increased peri-implant bone density because of loading. Crestal bone modification with SPS implants happen in relation to the machined collar area, as an outcome of a

combination of ‘‘stress shielding’’ of bone adjacent to the collar and remodeling needed to reform ‘‘biologic width.’’ As a result, there seems to be no need to use lengths greater than 7 mm with SPS implants. A review done by Hagi et al.,[10] focused on the outcomes using short (< 7 mm) endosseous dental implants in partially edentulous patients, because generally threaded dental implants do not usually perform well in short lengths (< 10 mm).

Machined-surface implants demonstrated higher failure rates than textured-surface implants; except for the sintered porous-surfaced implants, 7 mm long seem to have greater failure rates than those greater than 7 mm in length. And with textured-surface implants, higher failure rates were seen in the maxilla more than in the mandible. Whereas, with machined surface implants there was no difference in failure between maxillary and mandiblular arches.[1]

The implant has two different surfaces: a smooth polished collar on the coronal surface that is in contact with soft tissues, and a porous surface. The smooth surface requires a simple surgical approach that is either 1.0 mm or 2.0 mm in height to prevent plaque accumulation and it allows for situations in which absence of bone in one aspect prevents the implant from being totally submerged within bone. Clinical trials have shown no further bone loss if the porous part is not totally submerged into bone and the remainder of the implant is covered by a porous surface. These surfaces are designed to be biocompatible with the adjacent tissues. As a result of the weak support and stresses subjected to this area, bone remodeling occurs, and a net crestal bone loss occurs adjacent to the porous surface above the implant region. Many studies have shown that the amount of bone loss is controlled and it advances towards the junction between the

smooth surface and porous region, and creates no major change in the crestal bone geometry. These studies have also revealed that this small change in the crestal bone is due to the low forces applied to this area, because it is incapable of transferring stresses from the implant to bone through the smooth surface area. The amount of bone loss is around 1 mm for an implant with 1mm smooth coronal surface. The change in the coronal surface seen with Endopore implants is not greater than that seen with other dental implants.[1]

The porous surface helps in bone contact and is formed by sintering the titanium Ti-6Al-4V alloy powders of particle size 44 μm to 150 μm on a solid titanium surface forming the porous implant surface. It forms a two- to three-particle thick zone that forms a part of the implant unit. Sintering is a diffusion process that leads to bonding of the particles to each other and to the titanium substrate surface using high temperature and controlled atmosphere. It does not include melting the titanium but involves a solid-state diffusion that leads to particle-particle and particle-substrate junctions to make and maintain interconnected openings all over the sintered surface. The pores are of suitable size "50-200um" for bone and fibrous tissue to grow.[1] The proper selection of the particle size, sintering temperature, and sintering time leads to the formation of the opened pore structure while forming the desired mechanical integrity of the particles junctions. It has a multilayered surface with pores ranging from 50 μm to 200 μm with 35-volume-percent porosity; and thickness of the porous area around 0.3 mm with a surface area that ranges around 512 mm to 638 mm, the highest surface area/unit implant length of the implant systems that allows for faster bone formation during initial healing than threaded implants. One of the early studies researched the effect of the size of the

pore on the rates of bone ingrowths and interface strength and showed that pores ranging from 50 μm to 300 μm in size lead to the most rapid and fast rate of bone interface shear strength formation.[1] Histological studies of tetracycline-labeled samples taken from human implanted Endopore showed normal bone remodeling through the 0.3 mm-thick porous surface area specifying that appropriate blood supply was available for the bone formed in the porous area. This maybe noteworthy in that it implies the ability of the grown tissue to support a host defense response against microbial challenges in the area.[1] [14] Animal studies also indicated that fibrous and osseous tissues infiltrate all regions, while bone did not necessarily appear in the entire porous surface. The interconnected zone shows the structure of cancellous and cortical bone. Allowing appropriate vascularization in all areas of the porous surface is important to assess the long-term stabilization of the tissues.[1]

Examining the prepared metallographic samples across the porous structure show sinter necks that are similar to the Ti6A14V. The sintering procedure shows a more realistic method for forming a network of pores within the implant that allows bone to grow after placing the implant.[1] This leads to the formation of a biological bond of implant to bone that is able to withstand forces of occlusion, compressive, shear and tensile stresses. Animal studies have shown that initial implant stabilization results from the ability of 3-dimensional integration of initial pre-mineralized tissue with the porous implant surface and aids in bone formation, so osseointegration forms in a much shorter time and mechanical interlocking with bone. Even with the presence of micro movement in the healing phase, it favors bone formation within the implant pores.[1] Some animal studies showed that initial movements of 50 μm can be put up with without influencing

the rate of bone growth. Nevertheless, early loading should be avoided in implant placement allowing fast problem-free osseointegration.[1] A variety of implant surface designs are available including machined, grit based, acid etched, and plasma sprayed surfaces, as well as a combination of surface treatments. The irregular rough surface allows bone to implant interlock and provides resistance to interfacial tensile forces. Bone grows and forms into surface depressions or intrusions, and not in openings on the implant surface zone. Both transverse and vertical stresses work on dental implants during motion and during the healing stage after implant placement, and there is little resistance against the tensile stresses at the junction caused by transverse tipping forces. Consequently long periods and long implants are needed in order to allow reliable implant performance.[1, 4]

When comparing the Endopore implant with the threaded type in animal studies, the Endopore showed increased surface area of osseointegration, and it demonstrated that it allows the placement of short length implants to support prostheses. In other words, the Endopore implant can be used in cases where implants were not recommended due to absence of bone or to their proximity to vital structures.[1, 4]

Studies on animals showed some bone loss for threaded cylindrical implants but no bone loss has been observed for porous truncated coated implants. A clinical study on the Endopore system revealed that the greatest bone remodeling " mean loss = 0.44 mm" occurred in the first year of function, "mean loss = 0.14 mm" occurred between the first two years, and "mean loss = 0.17 mm" occurred between the second and third years, but no further loss occurred beyond that time.[1] This remodeling did not extend beyond the junction between the collar and the body of the implant.[1] A prospective study examined

the factors affecting the successes and failures of 1,003 pure titanium dental implants placed from 1987 to 2002 and were followed to 2003. Success rates were affected mostly by the age of the implant. Whereas, other factors like the patient age, gender, surface roughness of implant, site of placement, smoking, bone type, arch, screw versus press-fit, diameter, length, manufacturer, reason for tooth loss, site bony augmentation, placement timing, one- versus two-stage placement, or torque testing of implants did not significantly affect rate of success. Seventy-five percent of failures occurred before restoration. Failure rates were diverse, and while the age of the implant was statistically important in calculating failure, male smokers, maxillary first molars, and type 4 bone had increased failure rates. The study also showed that threaded surface-roughened implants had the highest success rates.[25]

Another study examined two sintered porous-surfaced dental implant designs to compare methods of crestal bone remodeling during a 14-month functional period in healed extraction sites in dog mandibles. The control, or short-collar design, was a press-fit implant with a machined collar of 2-mm, while the rest of the implant has a sintered porous surface. The test or hybrid design (long-collar) had three coronal-machined threads, while the rest of the implant had a sintered porous surface. Standardized radiographs showed significantly less crestal bone loss (0.82 mm to 0.93 mm versus 1.45 mm to 1.5 mm) with the hybrid design, and a slower approach to a steady state (12 months to 14 months for the hybrid versus 7 months for the standard design). Morphometric assessment of back-scattered scanning electron micrographs showed that crestal bone loss was significantly less for the hybrid design but the lingual part of the implant. The addition of coronal threads to the implant with a sintered porous surface for

long-term osseointegration reduced the amount of crestal bone loss compared to a machined collar area.[21] A study done to obtain histometric measurements of bone and peri-implant mucosal tissue in contact with two sintered porous-surfaced designs. The short-collar design had a collar height (smooth coronal region) of 0.75 mm, while the long-collar model had a smooth coronal region of 1.8 mm. Implants were placed two per side in healed mandibular extraction sites of four beagle dogs using a submerged method. After four weeks, they were uncovered and used to support fixed partial dentures for up to nine months. Samples were taken and nondemineralized specimens were observed histometrically to see the most coronal bone-to-implant contact (BIC) using the micro gap as a reference and standard mucosal parameters of biologic width. Significant differences in first BIC were found between designs (1.97 mm for long-collar versus 1.16 mm for short-collar implants) for posterior implants but not for anterior ones (1.21 mm versus 1.38 mm; $p = 40$). If crestal bone loss involved sintered surface, fibrous connective tissue ingrowths were observed to replace lost bone. No significant differences in peri-implant mucosal measurements were found between the implant designs. Histometric data seen for bone contact showed no significant differences between the long- and short-collar implant designs.[26]

USES

AS AN ABUTMENT FOR OVERDENTURES

Dental implants with a sintered porous surface used for implant fixation are a predictable and effective means of retaining a mandibular over denture in patients with advanced mandibular ridge resorption. The first clinical studies carried by

Pilliar et al.[1, 4, 8] involved the placement of 156 implants in 52 patients. Three Endopore implants ranging from 7.0 mm to 10.0 mm in length were placed in the anterior part of the mandible of each patient. After ten weeks, the implants were exposed to allow the placement of the over denture abutments. The final over denture was inserted in approximately 14 weeks. Their results showed a 95-percent success rate four years post-function (8 out of 156 failed). No mobility or pain suggestive of implant failure was detected. A minimum of 0.44 mm crestal bone loss was found in the first year, 0.17 mm in the second year and 0.13 mm in the third year of the study; this bone loss occurred at the area between the collar and the body of the implant. There was no bone loss exceeding the porous coat of the implant.[1, 4, 8] This study was followed for up to 10 years by Deporter et al.,[13] whose results revealed a 10-year implant survival of 92.7 percent and mean annual bone loss after one year to be 0.03 mm.

REPLACING MISSING TEETH

Ultra short sintered porous surfaced dental implants are used to replace missing teeth. Dental implant surface structure is a major aspect to determine how well the implants function in lengths ≤7 mm. As threaded implants show higher failure rates in short versus longer lengths, sintered porous surfaced implants perform well in short lengths.[11] A prospective study was carried out on 20 patients (10 males and 10 females) ranging in age between 30 years to 60 years, in which a single implant (10.mm mean length) was placed in each individual, and then restored with a crown after a four-month healing period. Radiographs and periodontal measurements were taken; no failures were noted.[3] Another study examined 48 Endopore dental implants ranging from 7mm to 9 mm, which replaced 17 premolar teeth and 31 molars in the mandibles of 24 partially-

edentulous patients. Eighty-three percent were replaced by single crowns. After a mean functional time of 32.6 months (range: 8.2 months to 50.3 months), the implant survival rate was 100 percent, and radiographic assessment showed minimal to no crestal bone loss.[9] Another study placed 151 Endopore dental implants with a mean implant length of 8.7 mm (76.8 percent in the posterior maxilla) of 50 partially-edentulous patients. When re-accessing the area, the implants were osseointegrated and used to support fixed prostheses. The mean functional time was 34.6 months and the cumulative survival rate was 97.3 percent (4 implants had failed). Radiographic analysis showed that there were no significant changes in crestal bone levels after 6 months, 1 year, and 2 years in function. There were no correlations between crestal bone loss and the implant length (7 mm, 9 mm, or 12 mm), implant diameter (3.5 mm, 4.1 mm, or 5.0 mm), and the position of the implant.[7] In a clinical study done by Deporter et al.,[6] 26 sintered, porous-surfaced press-fit dental implants that were 5 mm long and had a coronal diameter of 5 mm were placed in 20 individuals to replace maxillary and mandibular molars. Failure rates measured after 8 years of function were14.3 percent for the maxilla and 0 percent for the mandible.

IN AREAS OF MAXILLARY SINUS PROXIMITY AND LOW LEVELS OF BONE

Using dental implants in the maxilla is much difficult than in the mandible and are least predictable. Short, porous-surfaced root-form dental implants are used with an indirect, osteotome-mediated sinus elevation to restore the posterior part of the maxilla when limited amount of bone is remaining " 3 mm."[1] This method helps control the posterior maxilla with minimal bone height below the sinus floor.

A study carried out by Rahmani et al.[14] investigated the healing phases of localized indirect osteotome-mediated maxillary sinus floor elevation in relation to the use of sintered porous-surfaced dental implants in rabbits. On one side of the maxilla of each of 28 rabbits an implant was placed with no bone graft material, while on the collateral side an implant was placed after first adding Bio-Oss graft particles to the osteotomy. Samples were taken for morphometric assessment after 2 weeks, 4 weeks, 6 weeks, and 8 weeks of healing to assess bone contact and bone ingrowths of the porous implant surface. All implants became osseointegrated by bone ingrowths into the porous implant area. Placing a graft did not lead to a significant increase in the measurements; greater bone contact and particularly bone ingrowths at the apical portion of the implants were observed as healing time increased.[14] A clinical study carried on 16 patients with a mean implant length of 6.9 mm and a mean functional time of 11.1 months showed 100 percent success.[11] Another study of 334 implants (Endopore) placed in 112 fully- and partially-edentulous patients who were followed for 3 years. A technique of spreading buccal and lingual plates with osteotomes to place these implants in proximity to the sinus of the posterior maxilla was used. When the maxilla was prepared, the implants could be successfully placed in areas having limited available bone. Success rates were 97.0 percent for implants stabilizing a mandibular over denture, and 94.8 percent for implants placed in partially-edentulous patients. Many times, sinus lift or other augmentation procedures can be avoided in the maxilla and mandible, allowing for less patient morbidity and for an implant reconstruction that is more affordable for the patient.[1] Another study also reported the use of short (primarily 7-mm-long) sintered, porous-surface implants to treat the posterior maxilla using the indirect, sinus lift

procedure. One-hundred-four Endopore implants were used in 70 patients. The mean subantral bone height before implant placement was 4.2 mm, and all implants were placed using hand osteotomes and a graft of bovine hydroxyapatite. After an average time in function of 3.14 years, two implants were lost. The study concluded that the use of short, sintered, porous-surfaced implants and localized indirect sinus lift is an approach to help manage the posterior maxilla with low preoperative subantral bone height around 5 mm.[12] A study carried out by Kermalli et al.[27] used threaded surface-washed and sand-blasted, and sintered porous surface implants. This study involved 62 patients who received 97 implants; the results showed an 80.4 percent success rate for the press-fit implant, 97.5 percent for implants used in the direct technique, and 96.6 percent for threaded implants used in the indirect technique. There was also a significant difference in the length of the implants used, with the press-fit implants being much shorter than the threaded type. Crestal bone loss was significantly lower for the press-fit (0.57 mm). Their study also showed that using dental implants with a sinus elevation procedure is a predictable treatment for a resorbed maxilla.[27]

ELECTRON BEAM MELTING IMPLANTS

Charles Deckard, University of Texas in Austin, in 1986[17] produced fully functional parts by adding sintered layers. The layers are formed by the use of a computer-controlled laser that melts the powder to cover the cross sectional aspect made by a computer design model. This research was funded by The National Science Foundation and he invented rapid manufacturing, and the DTM machine producing metal parts from metal powder.[17] Rapid manufacturing decreases lead-time and increases the build flexibility for low-volume production of tailored pieces of metal. At present, rapid

manufacturing technologies include laser sintering (SLS), laser micro-sintering, selective laser melting (SLM), three- dimensional (3-D) laser cladding, electron beam melting (EBM), and electron beam sintering (EBS).[17] The formation of personalized dental implants by EBM makes it possible to greatly produce customized dental implants, which have a porous surface that aids in better osseointegration. By producing the root form and the abutment as one piece that has the same shape as the patient's tooth, less fracture at the crown root interface is expected. It is simply done by scanning an existing tooth by computer tomography and then converting it to a computer-aided design for production by EBM. This may reduce surgery and recovery time, as well as being more cost effective, providing better osseointegration. In mechanical properties, EBM samples have ultimate tensile strength of 1,028 MPa and 14 percent in tensile strain, similar to the mechanical properties of wrought Ti-6Al-4V.[17] Selective electron beam melting (SEBM) has been used progressively to make Ti-6Al-4V titanium structures for orthopedic usage.[15]

The generation of porous titanium products by (SEBM) conquers problems associated with high chemical affinity of liquid titanium to atmospheric gases, which decreases ductility of the metal. A study was done to examine using a smooth compact and a porous Ti-6Al-4V device made by the SEBM technique as scaffolds for bone formation. Fifteen domestic pigs with skull defects were used and the SEBM-formed titanium implants were placed into those defects. Microradiographs and histomorphometric analyses were performed 14 days, 30 days, and 60 days after surgery in order to examine the direct contact between bone and implant surfaces, and to measure the ingrowths of osseous tissue into the porous structure. Bone ingrowth increased

significantly. After 14 days the outer parts of the implants were filled with new bone tissue (14 percent). After 30 days the bone volume inside the implants reached almost 30 percent, and after 60 days bone formation inside the implants was about 46 percent. During the study bone-implant contact was found around all implants: 9 percent around compact samples, and 6 percent around porous samples after 60 days. This experiment showed that highly porous titanium implants with excellent interconnectivity manufactured using the SEBM method were suitable scaffolds for bone in growth.[16] In another study (Ti6Al4V) were made by free-form-fabrication (FFF), and were used as produced or after machining, and compared with wrought machined Ti6Al4V. Examination of the surface properties was done by Auger electron spectroscopy (AES), depth profiles, and interferometry. After 6 weeks, the tissue response in rabbit femur and tibia was examined by using light microscopy and histomorphometry. The results showed that the chemical and mechanical properties of the wrought machined titanium and the electron beam-melted (EBM) material were within the ASTM F136 specifications. The produced EBM Ti6Al4V implants had increased surface roughness and thicker surface oxide and, with the exception of a higher content of iron, a similar surface chemical composition when compared with machined EBM Ti6Al4V and machined, wrought Ti6Al4V implants. The implants had no difference in surface properties. The tissue response was similar for all three implant types. Histomorphometry showed a great degree of bone-to-implant contact for all the three implant types. The present results show that the surface properties of EBM Ti6Al4V display biological short-term behavior in bone equal to that of conventional wrought titanium alloy.[16]

Microcomputer tomography (microCT) studies show the ability to form three-dimensional structures with an interconnected porosity and pore sizes appropriate for tissue ingrowth and vascularization. Mechanical properties of the examined specimens, such as compressive strength and elastic modulus, were quite similar to the properties of human bone. Due to a lower strength difference between implant and bone, stress shielding effects after implantation might be prevented. Changing the chemical surface using HCl and NaOH induced bone creation *in vitro* bioactivity tests in simulated body fluid under active state. The modified bioactive surface is thought to aid in the stabilization of the implant and to enhance its long-term fixation.[28] A study was done by Li X et al.,[29] to measure the mechanical properties of a porous Ti-6Al-4V implants made by using the electron beam melting (EBM) method. X-ray diffraction (XRD) analysis to examine the specimens indicated that the EBM technique did not change the components of Ti-6Al-4V. The samples showed a Vickers micro-hardness value of approximately 428 HV. Compression and three-point bending tests were done to examine the mechanical properties of the 60-percent porosity of the Ti-6Al-4V implants. The compressive yield strength was 194.6 MPa, Young's modulus was 4.25 GPa, and ultimate compressive strength was 222.6 MPa, respectively. The bending stiffness was 3.7 GPa and bending strength was 126.3 MPa. The outcome of the study indicated that the porous Ti-6Al-4V implant with a low stiffness and high porosity could be used for biomedical applications.[29]

However, there has been very limited information about the *in vivo* performance of these implants. Moreover, the *in vivo* performance of EBM implants has never been evaluated side-by-side with commercially-available porous-coated press-fit implants.

MATERIALS AND METHODS

ANIMALS

Six healthy male New Zealand white rabbits (Myrtle's Rabbitry, Inc., Thompson Station, TN) weighing between 3.0 kg to 3.5 kg were used. *En bloc* samples were obtained 6 weeks following surgical placement of the implant for histological, histomorphometric, and mechanical testing. The Institutional Animal Care and Use Committee (IACUC) at Indiana University, Indianapolis, Indiana, USA approved the study.

IMPLANTS

Two implant types were used. Twelve Endopore (Innova Corp.) dental implants 5mm long and 3.5 mm wide were used as controls. Twelve Electron beam melting (EBM) dental implants 5 mm long and 3 mm wide made using Ti6Al4V ELI (ASTM Grade 23) were used as a testing group. They were designed and manufactured by Southern Methodist University.

SUGICAL PROCEDURE AND IMPLANT INSERTION

The implantation surgeries were done under sterile conditions. On the day of surgery, Meloxicam (Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO) (0.2 mg/kg SC) was administrated 40-60 minutes before the procedure as an analgesic drug. At the time of anesthesia, the animals were induced by Acepromazine (Butler Animal Health Supply, Dublin, OH) plus Torbugesic (Fort Dodge Animal Health, Fort Dodge, IA) (Ace

0.6mg/kg + Torb 0.75mg/kg). After initial induction, the anesthesia was maintained using Isoflurane (Butler**)** (3.5% at 1.5 l/m) via gas mask. Baytril (Bayer HealthCare LLC, Animal Health Division, Shawnee Mission, KS) 4 mg/kg SC was given as a prophylactic antibiotic. Following onset of anesthesia, hair over both hind limbs was clipped with electric clippers using #40 blades. Skin was disinfected with Betadine **(**Butler) and alcohol and the surgical site was draped with a sterile cloth. The rabbits were placed on a sterile cloth on top of a warm water-circulating blanket. Implants were inserted in a standard fashion. Holes were drilled with sharp drills (the drill was not used for more than 10 times) at low drill speeds under copious irrigation with saline solution. Four implants (two from each type) were placed in each rabbit; two implants from the same type were placed in each tibia. All implants were sterilized by autoclaving. Two implants were carefully pushed into the medial tibia at a distance of 11 mm apart. The soft tissues were closed in layers using 4-0 Vicryl (Ethicon, Inc. (A Johnson & Johnson Company, Somerville, NJ) in a subcuticular pattern to contain the implant. The procedure was repeated on the contralateral side.

POST-SURGICAL PROCEDURES

The animals were allowed full weight-bearing activity, water, and rabbit chow (Ralston Purina, Richmond, IN) *ad libitum*. They were monitored for any complications. After the surgery, Baytril (Bayer) 4 mg/kg SC was administered once daily for 4 days and Meloxicam (Boehringer) 0.2 mg/kg SC was given once daily for 2 days. Buprenex (Reckitt Benckiser Healthcare (UK) Ltd., Hull, England) was used at breakout pain (0.01-0.05 mg/kg SC, q8-24 hours). Animals were checked daily until the surgical wound healed. Body temperature, hydration status, activity, food and water consumption, and

conditions of operative site were examined. The suture material on the skin was removed on day 10 postoperatively. At 2 weeks and 1 week before sacrifice, calcein green (Sigma, St. Louis, MO) and alizarin red (Sigma) were injected at 10 mg/kg and 20 mg/kg through intramuscular injection.

After 6 weeks, the rabbits were sacrificed. At sacrifice, the rabbits were anaesthetized as described above and received an overdose of pentobarbitalum (Solfoton, ECR Pharmaceuticals, Richmond, VA) and natricum (Aventis Pharmaceuticals, Inc., Bridgewater, NJ) intravenously; lung puncture was performed in order to insure their death.

SPECIMEN RETRIEVAL AND HISTOLOGICAL PREPARATION

Specimens were retrieved from the right and left tibia. Twelve implants, 6 each of the Endopore (Innova Corp.) and EBM (Southern Methodist Univ.), were fixed for 48 hours in 10-percent phosphate-buffered formaldehyde solution in order to be used for histology analysis. The specimens were then embedded un-decalcified in polymethyl-methacrylate (PMMA). Five sections 50-μm in thickness were cut parallel to the long axis of the implant using a rotating microtome. Sections were placed on glass slides, coverslipped, and stained with toluidine blue (Sigma).

HISTOLOGICAL AND HISTOMORPHOMETRIC ANALYSIS

The slides were photographed and then evaluated at X10 and X20 using an automated histomorphometry system (Bioquant, Nashville, TN) under a light microscope (Nikon Eclipse 50i, Tokyo, Japan) equipped with a charge-coupled distributor camera

and connected to a computer (Dell Optiplex GX280, Round Rock, TX). Total implant perimeter in the first 3 mm into the cortical bone and the length in direct contact with bone were measured. Both the left and right side of the histology section were measured. Bone-to-implant contact (BIC) was obtained by dividing the total perimeter by the length in direct contact with bone and measured in micrometers. The mean values and standard deviations were calculated for the implant groups.

Using fluorescent light microscopy, fluorochrome analysis was performed on sections left unstained and examined with ultraviolet illumination. Mineral apposition rate (MAR) was calculated by measuring the distance between the edges of two consecutive labels divided by the number of days. The number of areas available for measurement and the mean value of the measurement may differ with the length of the labeling interval.[30] Three different areas were measured: away from the implant, next to the implant, and the posterior tibial border. The mineral apposition rate was calculated in (μm/day) units.

PUSHOUT TEST

Twelve specimens were used to examine the mechanical properties of the implants and were stored in saline at 4°C until testing. A pushout test was conducted to test the effects of implant type on bone ingrowths. A pushout jig was constructed.[31] (Figure 2). The specimen was placed on a support jig with clearance for the implant at least 0.7mm to minimize non-uniform stress distribution. Accurate alignment among the plunger, the specimen, and the support jig was essential to prevent the implant from jamming within its track of exit. The specimen was seated on the support fixture. The specimens were cemented to the support jig to assure ideal fit and alignment.[31] The

sample was loaded at a rate of 1 mm/min. Load was applied to the implant through the plunger connected to the crosshead of the materials testing machine and a force-displacement curve was recorded. The peak pushout force (F) was recorded in Newtons (N) and the apparent shear stiffness (E') was obtained from the slope of the load-displacement cure in its linear region.[31]

After the pushout test the specimens were examined under SEM. The samples were prepared by fracturing off only half of the bone at the bone-to-implant junction and leaving the implant on the bone. Then the samples were sputter coated with gold. The specimens were then embedded un-decalcified in PMMA. Five sections 50 μm in thickness were cut parallel to the long axis of the implant using a rotating microtome. Sections were stained with toluidine blue (Sigma).

STATISTICAL ANALYSIS

Mean histomorphometric and biomechanical values were calculated and recorded along with their standard deviations for each implant in each subject. Statistical analysis was performed using the paired t-test. A p-value of < 0.05 was set for significance.

RESULTS

IMPLANT

SEM of the Endopore (Innova Corp.) implant surface (Figure 3) shows spherical beads with size ranging from 39 μm to 134 μm, the average being 82±26 μm. The EBM (Southern Methodist Univ.) dental implant surface appears to have a smaller bead size, ranging from 28 μm to 81 μm, with an average size of 47±12 μm. The beads in the EBM (Southern Methodist Univ.) implants appeared rougher and more irregular than those seen in Endopore (Innova Corp.).

CLINICAL OBSERVATIONS

The rabbits showed uneventful healing throughout the 6-week experimental time period. None of the implants showed clinical signs of mobility or inflammation. From radiographic and clinical aspects, all implants appeared to have osseointegrated.

HISTOLOGY

For both EBM (Southern Methodist Univ.) and Endopore (Innova Corp.) implants, gross examination of the light microscopic sections revealed periosteal and endosteal callouses in close proximity to the implant; however, there were no signs of inflammation or soft tissue encapsulation around implants (Figures 4 and 5). A clear demarcation was noted between the original cortical bone and new bone growing in between the threads. The original cortical bone was clearly defined by its compact, lamellar appearance and by the presence of osteons; whereas the bone growing between implant and original cortical bone appeared to be less organized, less lamellar, and

appeared to be consistent with woven bone. In the Endopore (Innova Corp.) implant, some areas of resorption were seen followed by new bone formation. The resorption was likely due to the close proximity of the implant beads. In the EBM (Southern Methodist Univ.) implant, it can be seen that there were some loose metal beads that migrated into the tissue. This does not seem to have caused any inflammatory reaction in the surrounding bone. Bone that had grown into the porous space between the beads was also observed (Figure 6).

Mineral apposition rate to measure the amount of new bone formation was calculated in three different areas for both the EBM (Southern Methodist Univ.) and Endopore (Innova Corp.) samples, and showed no significant statistical difference between the two implants (Table I, Figure 7).

BONE TO IMPLANT CONTACT

Results of the bone to implant contact analysis are shown in Figure 8. A comparison between the Endopore (Innova Corp.) and the EBM (Southern Methodist Univ.) implant demonstrated similar bone-to-implant contact (BIC). The mean BIC for the Endopore (Innova Corp.) implant was approximately 35% ± 6% while the mean BIC for the EBM (Southern Methodist Univ.) implant was 32% ± 9%. Although the BIC value tended to be higher for the Endopore implants, it failed to reach statistical significance ($p > 0.05$).

PUSHOUT TEST

A typical load-displacement curve of the test sample is shown in Figure 9. The peak pushout force for Endopore (Innova Corp.) implants ranges from 112 N to 269 N,

with an average of 198.80 ± 61.29 N. The peak pushout force for EBM (Southern Methodist Univ.) implants was higher, ranging from 188 N to 379 N, with an average of 243.21 ± 69.75 N (Figure 10).

The apparent shear stiffness between bone and implant for the Endopore (Innova Corp.) implants ranges from 366 N/mm to 691 N/mm with an average of 577.36 ± 129.99 N. The apparent shear stiffness for EBM (Southern Methodist Univ.) implants was higher, ranging from 352 N/mm to 782 N/mm with an average of 584.48 ± 146.63 N (Figure 11). Neither the peak pushout force nor the apparent shear stiffness of the implants was statistically different between the two groups.

SEM images taken of the Endopore (Innova Corp.) implant surface after removing the bone at the implant bone junction show parts of bone attached between the implant beads (Figure 12). On the apposing bone surface, a replica of the implant beads can be seen indicating that bone grows around the titanium spherical beads (Figure 13). SEM images of the EBM (Southern Methodist Univ.) implant surface show smooth areas where beads have been pulled away when the bone was fractured and areas where bone is attached between the beads (Figure 14). Looking at the fractured bone surface we can see many implant beads remaining on the surface, as well as areas that are an indentation of the implant surface (Figure 15). The EBM (Southern Methodist Univ.) fracture specimen showed the direction of the pushout test to be downwards on the implant; the indentation of the implant on bone could also be seen. Part of the bone attached to the implant at the area of fracture; as well, part of the implant is still attached to bone (Figure 16).

FIGURES AND TABLES

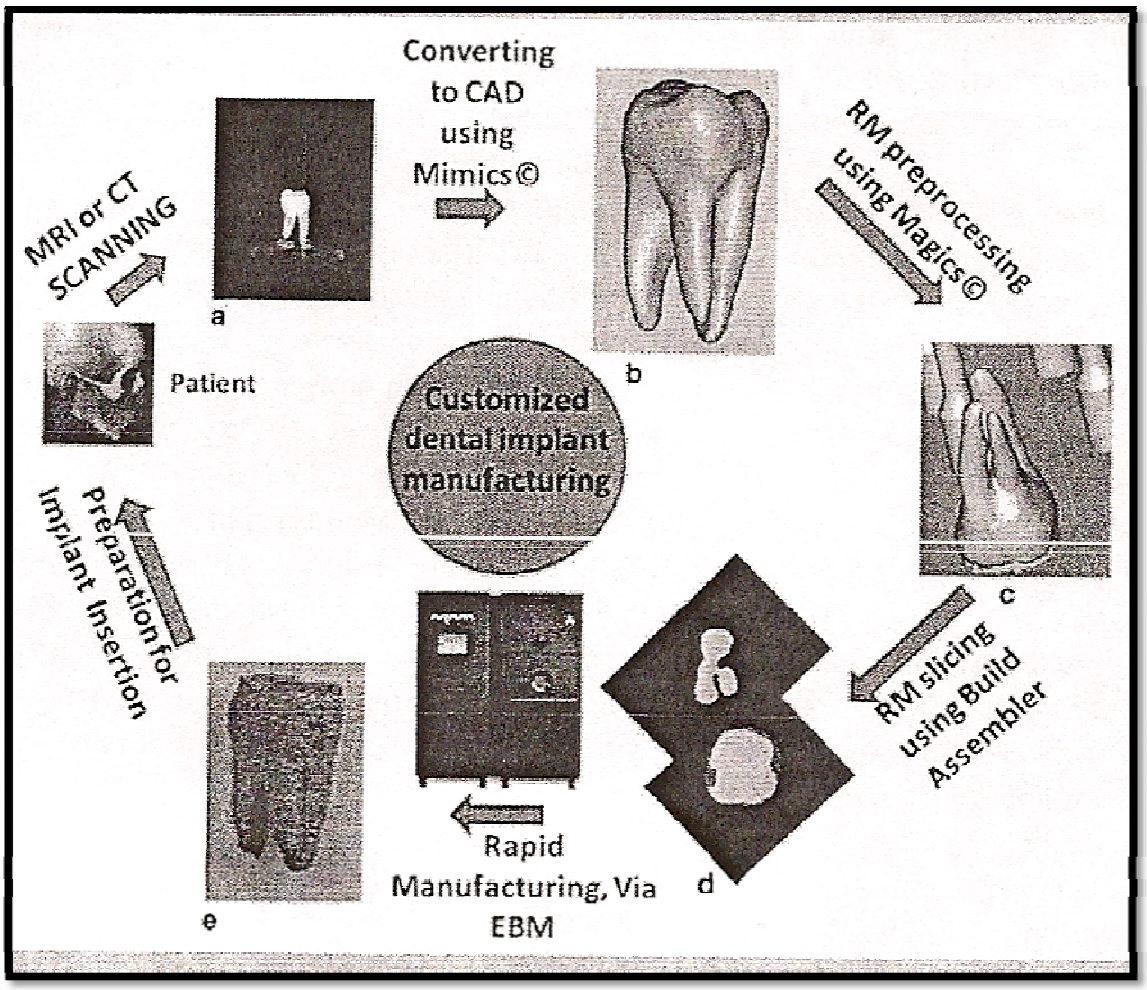

FIGURE 1. Steps for producing customized EBM dental implants.[4]

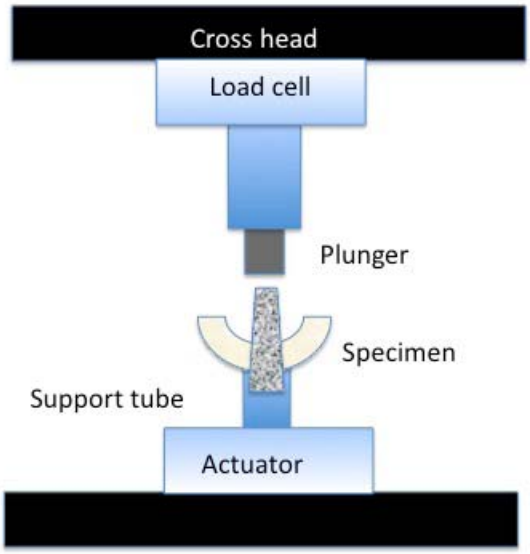

FIGURE 2. Schematic of a typical mechanical test fixture used in the pushout test. The support tube has an inner diameter greater than the diameter of the implant creating clearance.

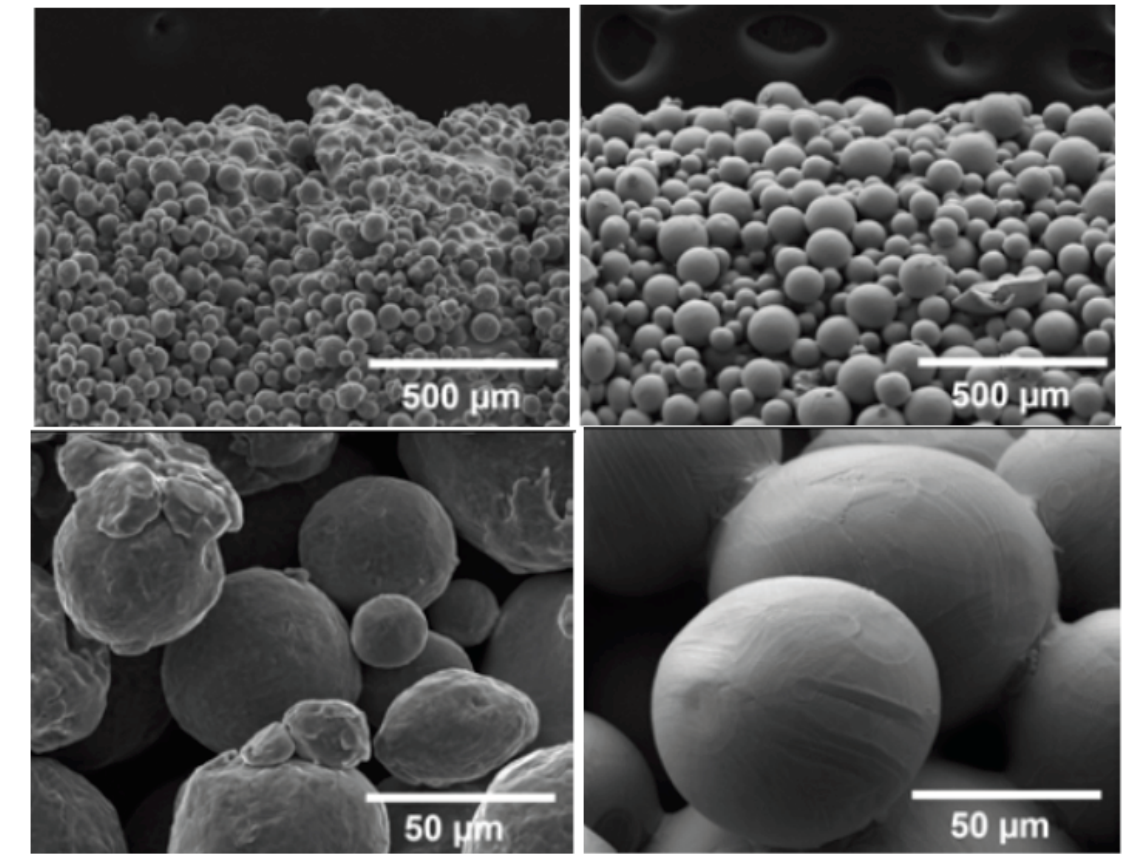

FIGURE 3. The surface of Endopore (Innova Corp.) (left) and EBM (Southern Methodist Univ.) [31] implants under SEM at X100 (top) and X1,000 (bottom).

FIGURE 4. Picture showing and overview of the osseointegrated Endopore (Innova Corp.) (left) and EBM (Southern Methodist Univ.) [31] implant. There are no signs of inflammation and soft tissue encapsulation around implants.

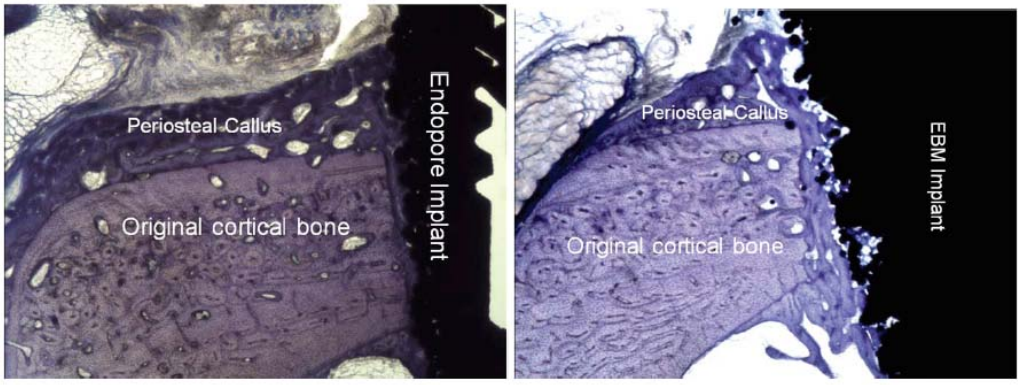

FIGURE 5. Picture showing periosteal callus overgrowth on Endopore (Innova Corp.) (left) and EBM (Southern Methodist Univ.) [31] implant under X2.5 magnification. There are no signs of inflammation or soft tissue encapsulation around implants.

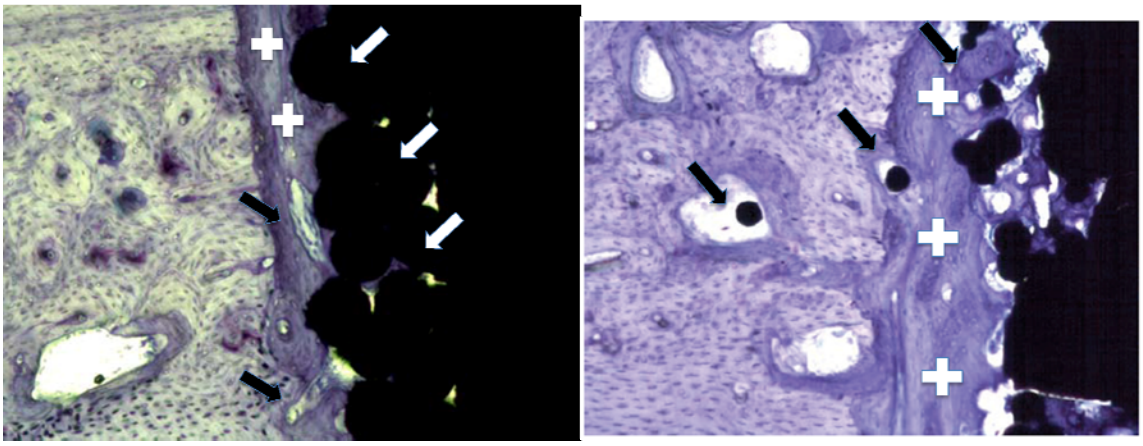

FIGURE 6. Picture showing new bone layer (+) formed between implant and the original cortical bone, Endopore (Innova Corp.) (left) and EBM (Southern Methodist Univ.) [31] implant under X10 magnification.

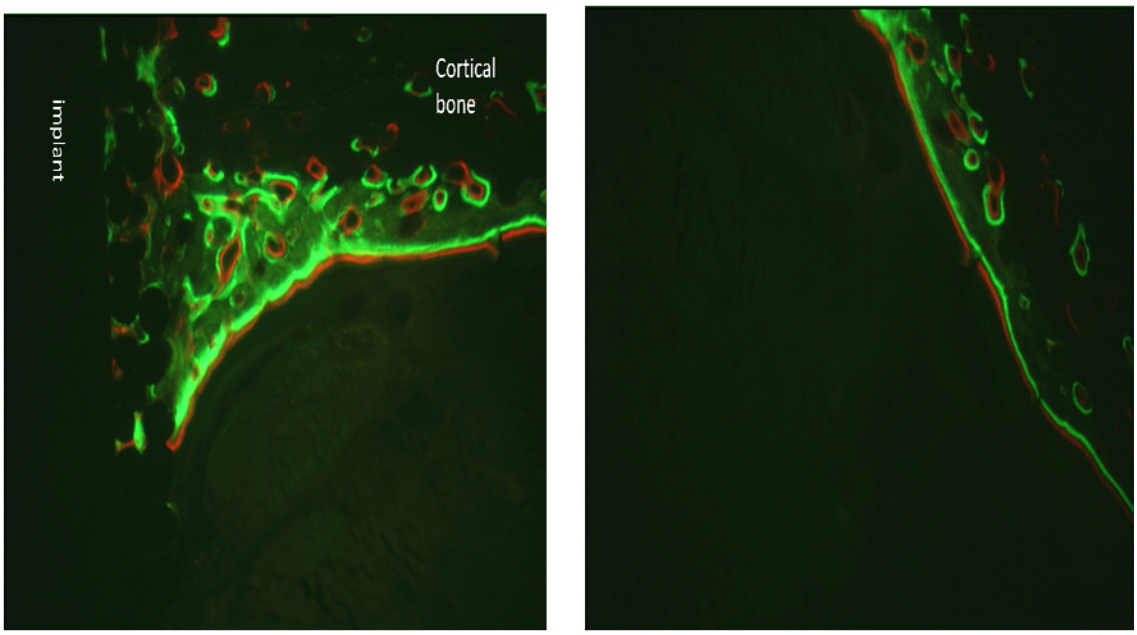

FIGURE 7. Fluorescent microscopy images (X4) were used to measure the mineral apposition rate. The fluorochrome labels used were calcein (green) (Sigma) and Alaziran (red) (Sigma). The implant bone interface can be seen on the left and the border of cortical bone is visible on the right.

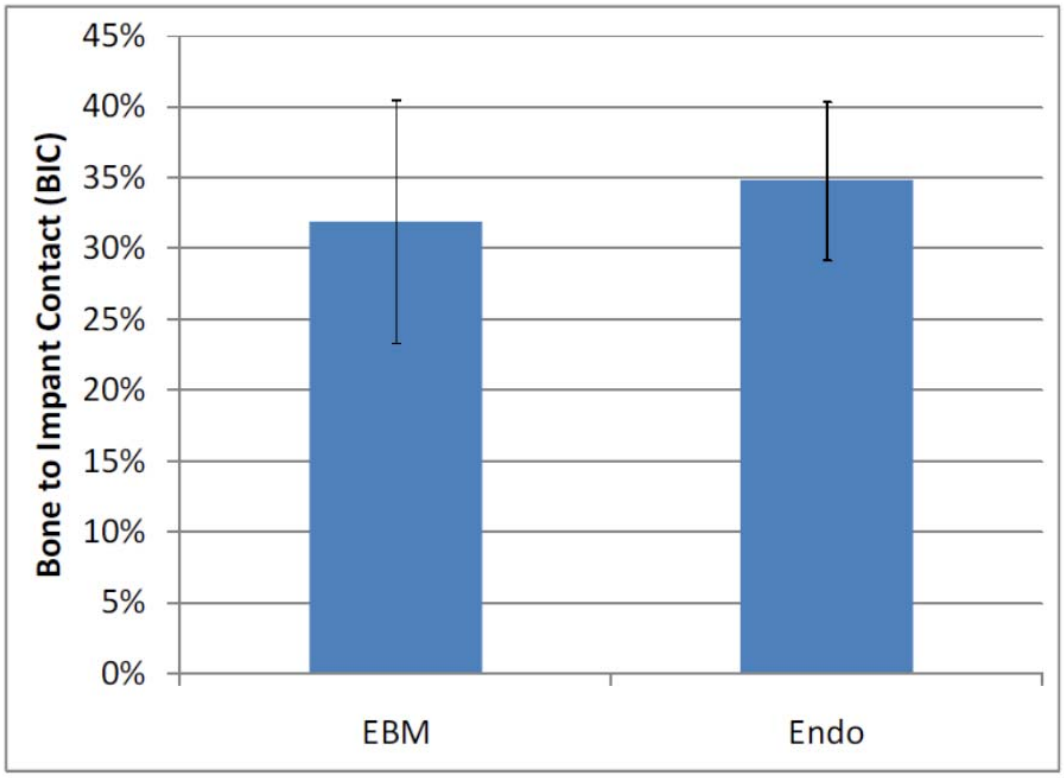

FIGURE 8. Chart showing the bone-to-implant contact (BIC) of EBM (Southern Methodist Univ.) and Endopore (Innova Corp.) implant.

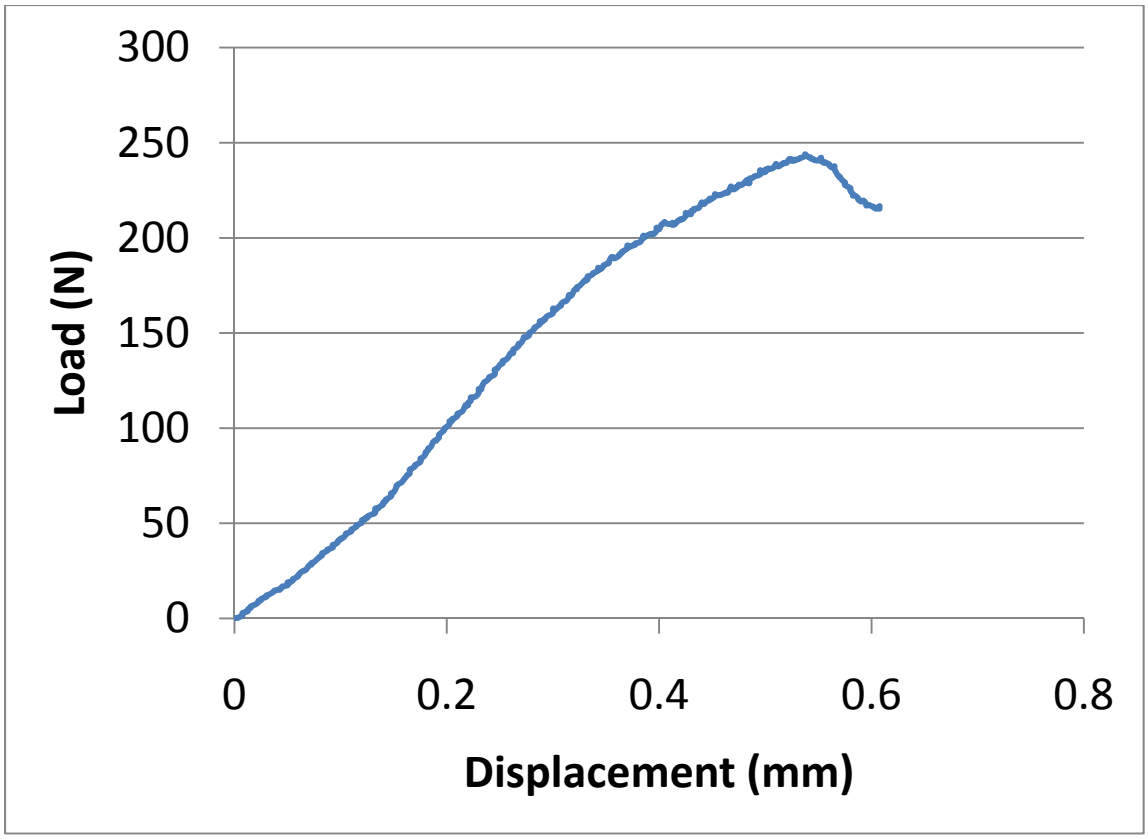

FIGURE 9. Chart showing a typical load-displacement curve from the pushout test.

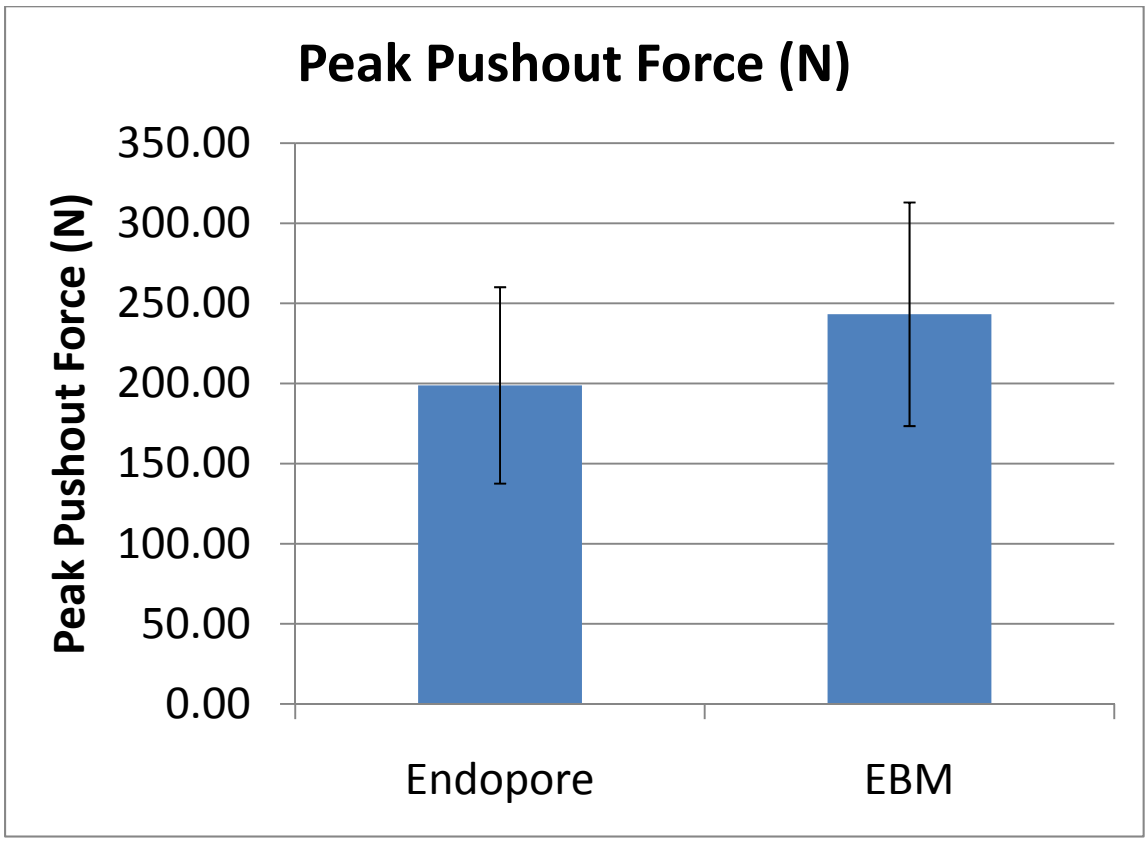

FIGURE 10. Chart showing the pushout force from Endopore (Innova Corp.) and EBM (Southern Methodist Univ.) implants.

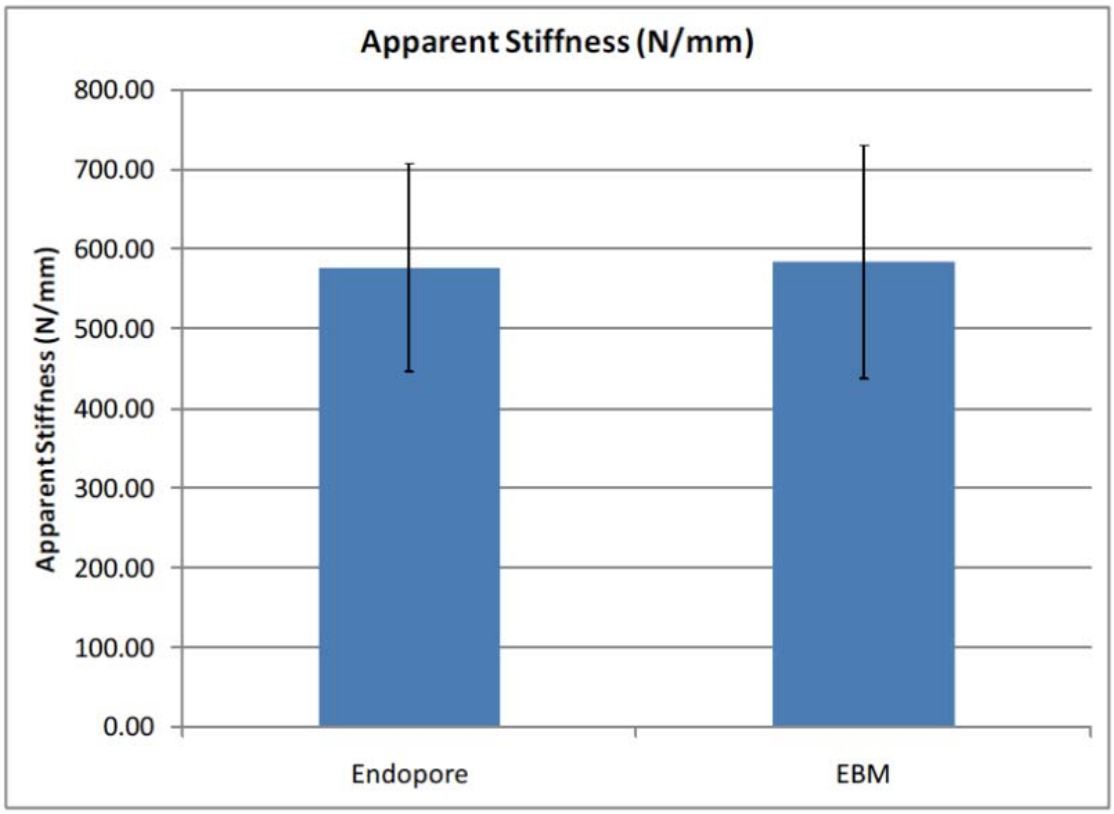

FIGURE 11. Chart showing the apparent shear stiffness from Endopore (Innova Corp.) and EBM (Southern Methodist Univ.) implants.

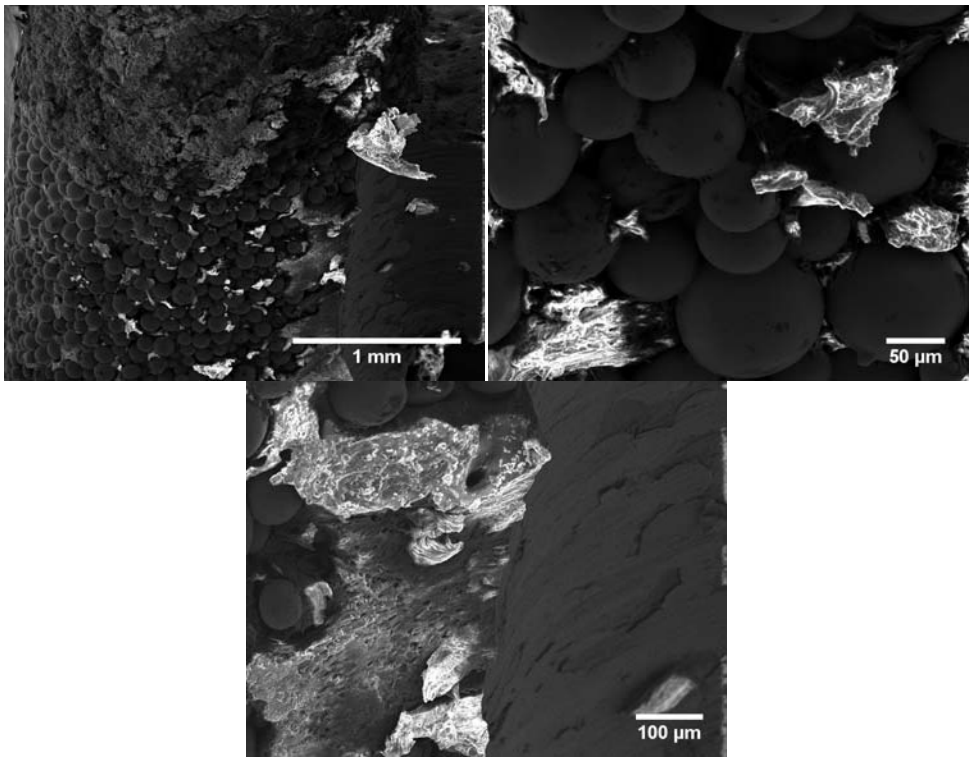

FIGURE 12. SEM Images of Endopore (Innova Corp.) implant surface after fracturing the bone at the implant bone junction: X50 (top left); X200 (bottom) shows the implant on the left and bone on the right; and at X350 (top right) bone pieces can be seen between the titanium implant beads.

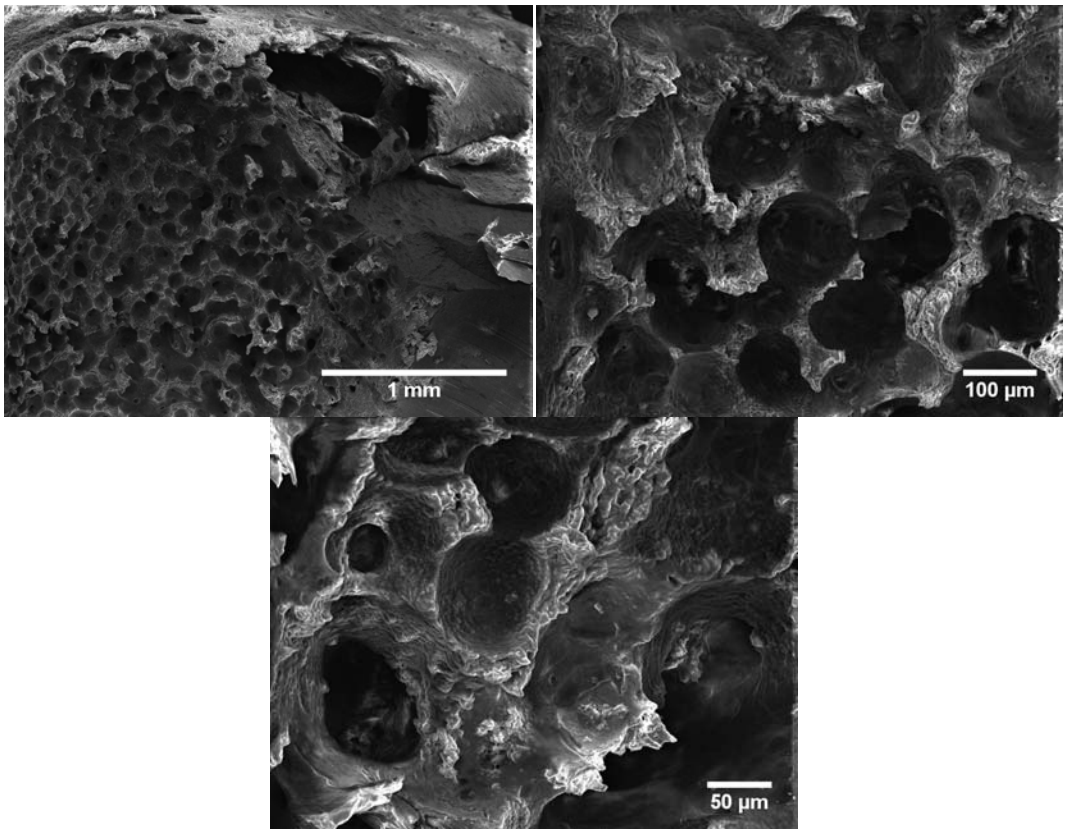

FIGURE 13. SEM images of the fractured bone surface apposing an Endopore (Innova Corp.) implant. At X50 (top left) the replica of implant beads formed by bone can be seen. The bottom view (X200) shows how bone grows around the titanium beads. And at X350 (top right) the bone surface is more clearly seen.

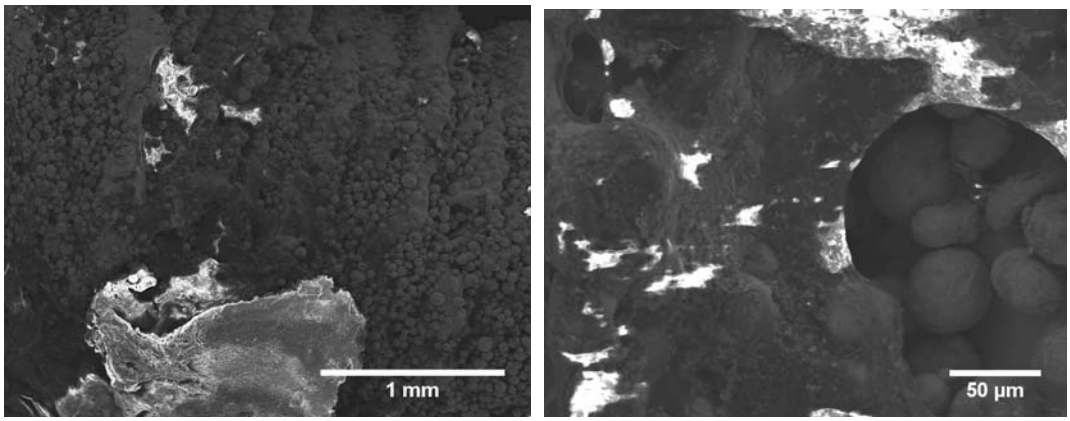

FIGURE 14. SEM images of EBM (Southern Methodist Univ.) implants after bone removal at the implant bone interface: At X50 (left), and more so at X500 [31], smooth areas appear on the implant surface where beads had been pulled away with the bone.

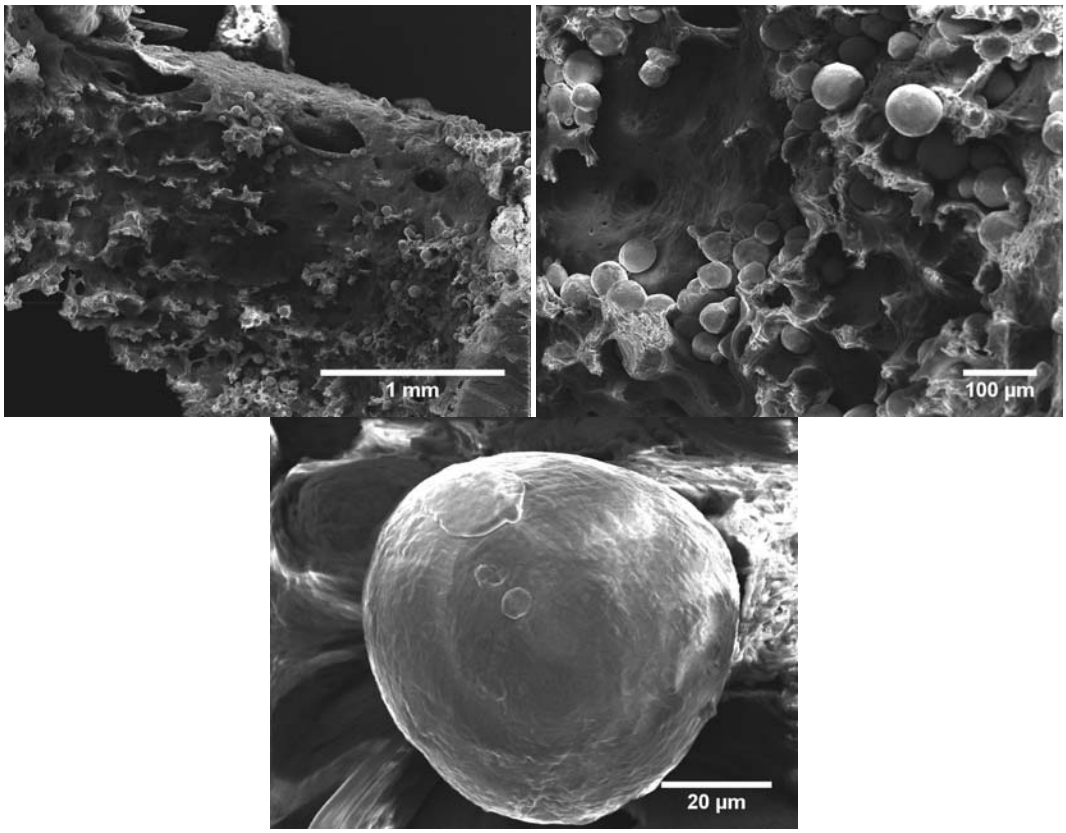

FIGURE 15. SEM images of the fractured bone surface apposing the EBM (Southern Methodist Univ.) implant. At X50 (top left) and X200 (top right) many titanium beads are attached to the bone surface. At X1500 (bottom) a fractured bead left on the bone is visible. The original attaching point can be seen on the upper left of the bead.

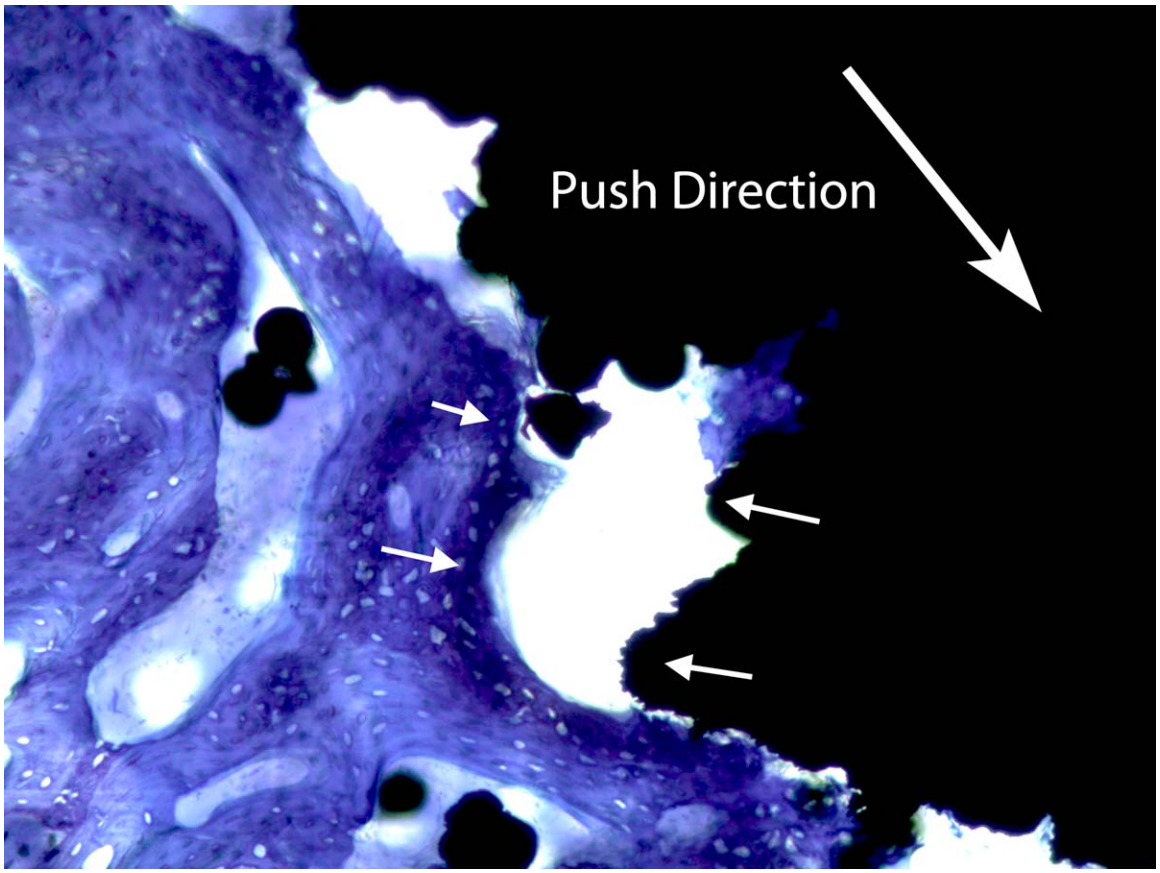

FIGURE 16. Histological picture of EBM (Southern Methodist Univ.) implant after pushout test. The direction of the pushout test is indicated by the large white arrow and the indentation of the implant on bone is indicated by the smaller white arrows. Note that part of the bone is attached to the implant at the area of fracture and part of the implant is still attached to bone as well.

TABLE I

Mineral apposition rate (μm/day) measured in fluorescent samples. Values displayed as mean ± standard deviation. No statistical significance was found between the two types of implants.

	Away from implant	Next to implant	Posterior tibial border
Endopore	2.80± 0.90	2.99 ±1.19	3.09 ±0.88
EBM	2.78 ±1.05	3.00 ± 1.04	2.96 ± 0.99

DISCUSSION

Porous-coated press-fit implants have been successful in certain clinical applications. Many clinical studies done on the commercial porous-coated press-fit implant system (Endopore) show high success when used as short implants.[1, 2] They have been successfully used as abutments for over dentures,[1, 3-5] replacing missing teeth, especially in narrow areas,[6-10] and in areas of maxillary sinus proximity and low levels of bone.[4, 8, 11-14] It has a multilayered surface with pores ranging from 50 μm to 200 μm with 35 volume percent porosity. The thickness of the porous area is around 0.3 mm and the surface area ranges between 512 mm and 638 mm, which is the highest surface area/unit implant length of the implant systems that allows for faster bone formation during initial healing than threaded implants.

On the other hand, rapid manufacturing[33] is a novel processing method developed over the last two decades. Electron Beam Melting (EBM) has been used to make porous Ti-6Al-4V titanium structures for orthopedic applications. EBM has been used to make personalized dental implants with a porous surface that provides better osseointegration.[16] This may reduce surgery and recovery times and could be more cost effective. The early *in vitro* studies showed great biocompatibility, good mechanical properties, and a good potential for bone in growth. However, the *in vivo* performance of EBM implants has never been evaluated side-by-side with commercially-available porous-coated press-fit implants.

The results from this study confirmed the *in vivo* biocompatibility of the EBM (Southern Methodist Univ.) dental implants. No adverse effects were seen, and animals

had normally recovered after surgery. After 6 weeks of implantation, the implants were well integrated in the surrounding bone and showed new bone penetrating into the porous space.

There are various methods used for the evaluating bone growth into porous structures. Two-dimensional (2D) image analysis is usually used to measure the amount of bone in the pores and to analyze the bone-implant contact by measuring the contact lines between the Ti and bone by optical, radiographical techniques, or SEM.[34] Though many clinical studies were published on the use of Endopore in clinical situations, not many animal studies have been reported. In our study we calculated the bone-to-implant contact in both Endopore (Innova Corp.) and the EBM (Southern Methodist Univ.) implants and found similar values. Our readings are slightly higher than those obtained by Rahmani et al.,[14] (22.8% ± 10.8) who measured bone contact and bone in growth of customized sintered porous-surfaced dental implants on one side of the maxilla of 28 rabbits after 8 weeks of healing. The difference in the readings could be due to difference in the implant shape, size and length the area where the implants were placed and the time the samples were retrieved. Their implants were customized and manufactured by Innova Corp., Toronto, Canada. The implants were cylindrical, 3 mm in length, 2 mm in diameter, and were placed in the bone underlying each of the right and left maxillary sinuses where the bone is more cancellous. Whereas our implants were tapered, 5 mm in length, 3mm in diameter, and were placed in the tibia where the bone is more cortical. Ponader et al.[16] measured the BIC in compact and porous titanium cylinders (8 mm long x 4mm diameter) prepared by selective electron beam-melting of Ti-6Al-4V powder using EBM S12 system (Arcam AB, Mölndal, Sweden) and placed in

skull defects of pigs. For the compact samples, BIC decreased from 29.27% ± 11.23% on day 14 to 18.78% ± 9.74% on day 30 and 8.98% ± 2.89% on day 60. Whereas, the BIC around porous samples was 0.47% ± 0.47% on day 14, 4.14% ± 4.14% on day 30, and 5.96% ± 1.36% on day 60. BIC decreases because of necrotic bone resorption opposite to the titanium surface reducing the mechanical stability of the implant and micromovements of the implant hinder bone formation.[16] Our results are within the range of the results obtained by De Riu et al,[35] where titanium implants were placed in sheep tibia with and without autologous bone grafts had a BIC of 29.54% ± 9.00% for grafted implants and 26.76% ± 5.00% for the controls after two months. In another study, titanium microimplants with machined and sandblasted acid-etched surfaces were placed in human maxilla. Two months after placement, the mean BIC was 20.66% ± 14.54% for the machined surfaces and 40.08% ± 9.89% for the sandblasted acid-etched surfaces[36] Because Endopore has performed well in clinical situations and our results show that EBM (Southern Methodist Univ.) has similar bone-to-implant contact as Endopore (Innova Corp.), we expect EBM (Southern Methodist Univ.) to have good compatibility as well.

Pushout test is regularly used to evaluate the mechanical proficiency of biological attachment of orthopedic implants through the measurement of the shear strength of the bone- implant interface. It measures the force needed to displace the implant from the surrounding tissue. When pushout data from various studies are compared, a large difference in data is seen, even of similar implant materials due to differences in bonding of bone and implant and also due to the dissimilarity in the ways of testing. Readings may also vary within a single test and prevent proper comparison of the data.[31] To our

knowledge, Endopore dental implants have never been evaluated by a pushout test. In our study, EBM (Southern Methodist Univ.) showed slightly higher pushout force and shear stiffness that was not statistically different from that of Endopore (Innova Corp.). Our data is consistent with the results from Boone et al.,[33] which measured the pushout force in the same animal model of different types of hydroxyapatite-coated polymer rods after 12 weeks implantation (120.7± 104.1 N).[33] Our readings were much lower than the readings obtained by Deglurkar et al,[37] who measured the interface stiffness in porous tantalum implants (Trabecular Metal, Minneapolis, MN) of three different groups inserted in the distal femur of rabbit models. Cell-culture disks machined the conventional way (2300 N/mm), machined using a wire EDM machine (Mitsubishi, Cypress, CA) (2500 N/mm) and TM disks, used as controls (1500 N/mm). The great difference could be due to the difference in the implant type, size (25 mm in length by 5 mm in diameter), location, and the way the test was conducted.[38] On the other hand, our shear stiffness values were much higher than those obtained by Jakobsen et al,[38] who measured the shear stiffness in cylindrical porous bead-coated implants (Ti-6Al-4V, ASTM F-136) with a diameter of 6.0 mm and length of 10.0 mm (DePuy Orthopaedics, Warsaw, IN) placed in the proximal part of dog humerous 6 weeks after insertion. That could be because a displacement rate of 5 mm/min with a 2500 N load cell was used, where we used a loading rate of 1 mm/min. Li et al.[39] measured the BIC and pushout force of grit-blasted Ti implants and hydrofluoric acid treated implants in ovariectomized rats 12 weeks after being implanted in the femur. Their mean BIC results are 20 percent for the untreated and 55 percent for the treated implants. Their pushout force measurements are 32.6 N ± 3.5 for the untreated and 71.7 N ± 10.2 for the fluoride

modified. Their readings for the BIC for the untreated model are lower than our results, as well as the pushout force for both models. This could be due to the difference in the animal model, the type of bone, and type of implant as they used grit blasted titanium implants.

Mineral apposition rate μm/day is used to measure the amount of new bone apposition during the healing period by administrating certain bone markers subcutaneously within the animals. Witte et al. [40] measured the MAR in the same animal model around open-porous scaffolds made of magnesium alloy AZ91D and compared the peri-implant bone remodeling around an autologous bone transplant in the opposite side after 3 months and 6 months.[40] They found MAR of 1.8 ± 0.2 μm/day after 3 months in the control side and 2.4 ± 0.4 μm/day on the magnesium scaffold side. Our data is slightly higher compared to the study by Witte et al.[40] That could be due to the difference in the area where the implants were placed as they placed their implants in the condyles of the knees while our implants were placed in tibia. Foley et al.[41] measured the BIC and MAR around acid etched titanium implants with phosphate coating that had been inserted in the mandibles of six foxhounds 12 weeks post implant placement. Their MAR results were lower than our readings, due to the difference in the animal model, type and size of implant, and implant location. Their BIC results were higher than our results for the same reasons as well as the difference in the way the BIC was calculated. Our results were similar to Clark et al.,[42] who calculated the average MAR of mechanically loaded titanium implants (5 mm was significantly greater than the average MAR of unloaded controls at 2.2 ± 0.92 μm/day ($P < 0.01$). A study by Wang et al.[43] measured the BIC, pushout force, and bone apposition rate of titanium implants placed in

cortical and cortico-cancellous bone of sheep femur for six weeks. The BIC and bone apposition rate results in were low compared to our results, whereas the pushout force was greater than the measurements we obtained, and their specimens were loaded at a loading rate of 10 mm/min with a 20 kN load cell. Another study was carried out using three types of cylindrical, 5 mm diameter, 25 mm long, fully porous-coated implants placed in rabbit knees. Their MAR readings, measured at 6 weeks after placement, were higher than our readings as was the the interface stiffness, which could be due to the use of larger and longer implants and the difference in the implant location, as well as the difference in the displacement rate of the pushout test (0.1 mm/ second).[32]

Within our study our results show similar range of MAR for the Endopore (Innova Corp.) and EBM (Southern Methodist Univ.) implants, suggesting bone remodeling behavior in both implant types.

In SEM and histology samples, we observed scattering of many small titanium particles in EBM (Southern Methodist Univ.), compared to Endopore (Innova Corp.) in freshly-retrieved and in mechanically-tested samples. In freshly-retrieved samples the particles could have been dislodged into the tissue at the time of implant placement. While in mechanically tested samples, they could have been dislodged from the implant surface at the time of testing. The loose titanium particles from EBM (Southern Methodist Univ.) could be a result of weaker bonding between particles. Whether the dislodged particles would become an issue in the long-term use will need to be investigated further.

SUMMARY AND CONCLUSIONS

In this study, we compared the *in vivo* performance of EBM (Southern Methodist Univ.) implant with a commercial porous-coated dental implant (Endopore, Innova Corp.) by evaluating the histology, bone-to-implant contact, mineral apposition rate, and mechanical properties of the retrieved samples. The histology evaluation shows osseointegration of surrounding bone with both implant types. Bone was found to grow into the porous space between the beads. There was no significant difference in the bone-to-implant-contact (BIC), nor mineral apposition rate (MAR) between the EBM (Southern Methodist Univ.) and Endopore (Innova Corp.) implants. In mechanical property evaluations, the peak pushout force and the apparent shear stiffness of EBM (Southern Methodist Univ.) were higher than the Endopore (Innova Corp.) implants. However, there were no statistical differences in these results. These results suggest that the implants manufactured by EBM (Southern Methodist Univ.) perform equally well with the commercial implant Endopore (Innova Corp.) in this current animal model.

REFERENCES

1. Pilliar RM, Deporter DA, Watson PA, Todescan R. The Endopore implant-enhancement osseointegration with a sintered porous-surfaced design. Oral Health 1998;88(7):61-4.

2. Stanford CM. Surface modifications of dental implants. Aust Dent J 2008;53(Suppl 1):S26-33.

3. Deporter D, Watson P, Pharoah M, Todescan R, Tomlinson G. Ten-year results of a prospective study using porous-surfaced dental implants and a mandibular overdenture. Clin Implant Dent Relat Res 2002;4(4):183-9.

4. Fleming AE. The Endopore dental implant system: implant treatment simplified. J Can Dent Assoc 1994;60(9):785-9.

5. Pilliar RM, Deporter DA, Watson PA, Valiquette N. Dental implant design—effect on bone remodeling. Jo Biomed Mater Res 1991;25(4):467-83.

6. Deporter D, Ogiso B, Sohn DS, Ruljancich K, Pharoah M. Ultrashort sintered porous-surfaced dental implants used to replace posterior teeth. J Periodontol 2008;79(7):1280-6.

7. Deporter D, Pilliar RM, Todescan R, Watson P, Pharoah M. Managing the posterior mandible of partially edentulous patients with short, porous-surfaced dental implants: early data from a clinical trial. Int J Oral Maxillofac Implants 2001;16(5):653-8.

8. Deporter DA, Todescan R, Watson PA, Pharoah M, Levy D, Nardini K. Use of the Endopore dental implant to restore single teeth in the maxilla: protocol and early results. Int J Oral Maxillofac Implants 1998;13(2):263-72.

9. Deporter DA, Todescan R, Watson PA, Pharoah M, Pilliar RM, Tomlinson G. A prospective human clinical trial of Endopore dental implants in restoring the partially edentulous maxilla using fixed prostheses. Int J Oral Maxillofac Implants 2001;16(4):527-36.

10. Hagi D, Deporter DA, Pilliar RM, Arenovich T. A targeted review of study outcomes with short (< or = 7 mm) endosseous dental implants placed in partially edentulous patients. J Periodontol 2004;75(6):798-804.

11. Deporter D, Todescan R, Caudry S. Simplifying management of the posterior maxilla using short, porous-surfaced dental implants and simultaneous indirect sinus elevation. Int J Periodontics Restorative Dent 2000;20(5):476-85.

12. Deporter DA, Caudry S, Kermalli J, Adegbembo A. Further data on the predictability of the indirect sinus elevation procedure used with short, sintered, porous-surfaced dental implants. Int J Periodontics Restorative Dent 2005;25(6):585-93.

13. Heller AL, Heller RL. Clinical evaluations of a porous-surfaced endosseous implant system. J Oral Implantol 1996;22(3-4):240-6.

14. Rahmani M, Shimada E, Rokni S, et al. Osteotome sinus elevation and simultaneous placement of porous-surfaced dental implants: a morphometric study in rabbits. Clin Oral Implants Res 2005;16(6):692-9.

15. Thomsen P, Malmstrom J, Emanuelsson L, Rene M, Snis A. Electron beam-melted, free-form-fabricated titanium alloy implants: material surface characterization and early bone response in rabbits. J Biomed Mater Res B Appl Biomater 2009;90(1):35-44.

16. Ponader S, von Wilmowsky C, Widenmayer M, et al. *In vivo* performance of selective electron beam-melted Ti-6A1-4V structures. J Biomed Mater Res A 2010;92(1):56-62.

17. Chahine G, Koike M, Okabe T, Smith P, Kovacevic R. The design and production of T1-6A1-4V ELI customized dental implants. JOM 2008;60(11):50-55.

18. Esposito M, Hirsch J, Lekholm U, Thomsen P. Differential diagnosis and treatment strategies for biologic complications and failing oral implants: a review of the literature. Int J Oral Maxillofac Implants 1999;14(4):473-90.

19. Misch CE. Contemporary implant dentistry. 3rd Ed. St. Louis: Mosby Elsevier, 2008.

20. Brånemark P-I, Zarb GA, Albrektsson T. Tissue-integrated prostheses: osseointegration in clinical dentistry. Chicago: Quintessence, 1985:305.

21. Zarb GA, Schmitt A. Osseointegration for elderly patients: the Toronto study. J Prosthet Dent 1994;72(5):559-68.

22. Porter JA, von Fraunhofer JA. Success or failure of dental implants? A literature review with treatment considerations. Gen Dent 2005;53(6):423-32, 433, 446.

23. Fraunhofer JAv. Scientific aspects of dental materials. London, Boston: Butterworths, 1975.

24. Lindh T, Gunne J, Tillberg A, Molin M. A meta-analysis of implants in partial edentulism. Clin Oral Implants Res 1998;9(2):80-90.

25. Lemmerman KJ, Lemmerman NE. Osseointegrated dental implants in private practice: a long-term case series study. J Periodontol 2005;76(20):310-9.

26. Deporter D, Al-Sayyed A, Pilliar RM, Valiquette N. “Biologic width” and crestal bone remodeling with sintered porous-surfaced dental implants: a study in dogs. Int J Oral Maxillofac Implants 2008;23(3):544-50.

27. Kermalli JY, Deporter DA, Lai JY, Lam E, Atenafu E. Performance of threaded versus sintered porous-surfaced dental implants using open window or indirect osteotome-mediated sinus elevation: a retrospective report. J Periodontol 2008;79(4):728-36.

28. Heinl P, Muller L, Korner C, Singer RF, Muller FA. Cellular Ti-6A1-4V structures with interconnected macro porosity for bone implants fabricated by selective electron beam melting. Acta Biomater 2008;4(5):1536-44.

29. Li X, Wang CT, Zhang WG, Li YC. Properties of porous Ti-6A1-4V implant with a low stiffness for biomedical application. Proc Inst Mech Eng H 2009;223(2): 173-8.

30. Parfitt AM, Drezner MK, Glorieux FH, et al. Bone histomorphometry: standardizationo f nomenclature, symbols, and units. Report of the ASBMR Histomorphometry Nomenclature Committee. J Bone Miner Res 1987;2(6):595-610.

31. An YH, Draughn RA. Mechanical testing of bone and the bone-implant interface. Boca Raton: CRC Press, 2000.

32. Willie BM, Yang X, Kelly NH, et al. Osseointegration into a novel titanium foam implant in the distal femur of a rabbit. J Biomed Mater Res B Apply Biomater 2010;92(2):479-88.

33. Boone PS, Zimmerman MC, Gutteling E, Lee CK, Parsons JR, Langrana N. Bone attachment to hydroxyapatite coated polymers. J Biomed Mater Res 2989;23(Suppl A2):183-99.

34. Wazen RM, Lefebvre LP, Baril E, Nanci A. Initial evaluation of bone ingrowth into a novel porous titanium coating. J Biomed Mater Res B Appl Biomater 2010;94(1):64-71.

35. De Riu G, De Riu N, Spano G, Pizzigallo A, Petrone G, Tullio A. Histology and stability study of cortical bone graft influence on titanium implants. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103(4):e1-7.

36. Grassi S, Piattelli A, Ferrari DS, et al. Histologic evaluation of human bone integration on machined and sandblasted acid-etched titanium surfaces in type IV bone. J Oral Implantol 2007;33(1):8-12.

37. Deglurkar M, Davy DT, Stewart M, Goldberg VM, Welter, JF. Evaluation of machining methods for trabecular metal implants a rabbit intramedullary osseointegration model. J Biomed Mater Res B Appl Biomater 2007;80(2):528-40.

38. Jakobsen SS, Baas J, Jakobsen T, Soballe K. Biomechanical implant fixation of CoCrMo coating inferior to titanium coating in a canine implant model. J Biomed Mater Res A 2010;94(1):180-6.

39. Li Y, Zou S, Wang D, Feng G, Bao C, Hu J. The effect of hydrofluoric acid treatment on titanium implant osseointegration in ovariectomized rats. Biomaterials 2010;31(12):3266-73.

40. Witte F, Ulrich H, Palm C, Willbold E. Biodegradable magnesium scaffolds. (Pt 2). Peri-implant bone remodeling. J Biomed Mater Res A 2007;81(3):757-65.

41. Foley CH, Kerns DG, Hallmon WW, et al. Effect of phosphate treatment of acid-etched implants on mineral apposition rates near implants in a dog model. Int J Oral Maxillofac Implants 2010;25(2):278-86.

42. Clark PA, Rodriguez A, Sumner DR, Hussain MA, Mao JJ. Modulation of bone ingrowth of rabbit femur titanium implants by *in vivo* axial micromechanical loading. J Appl Physiol 2005;98(5):1922-9.

43. Wang C, Karlis GA, Anderson GI, et al. Bone growth is enhanced by novel bioceramic coatings on Ti alloy implants. J Biomed Mater Res A 2009;90(2):419-28.

ABSTRACT

BONE REGENERATION IN NOVEL POROUS TITANIUM IMPLANTS

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The objective of this study was to evaluate the *in vivo* performance of the novel press-fit dental implant fabricated via electron beam melting (EBM, Southern Methodist Univ.) and compare it to a commercially-available porous-coated press-fit dental implant (Endopore, Innova Corp.).

Twelve cylindrical shaped implants 3 mm in diameter x 5 mm long were made by EBM (Southern Methodist Univ.) using Ti6Al4V ELI alloy. Twelve commercial implants (Endopore, Innova Corp.) of the same geometry were used as controls. Samples were implanted in rabbit tibia and retrieved six weeks postoperatively. Six specimens

from each implant type were embedded undecalcified, sectioned, and stained with toluidine blue (Sigma) for histomorphometry analysis. Bone-to-implant contact (BIC) was measured. On the six remaining samples from each implant type, the mechanical properties were evaluated by pushout test on a material testing machine. The samples were loaded at a loading rate of 1 mm/min. The pushout strength was measured and the apparent shear stiffness was calculated. The results were analyzed with a paired-t test.

The histology shows osteointegration of surrounding bone with both implant types. Bone was found to grow into the porous space between the beads. Both the Endopore (Innova Corp.) and the EBM (Southern Methodist Univ.) showed similar BIC. The mean BIC for the Endopore (Innova Corp.) and EBM (Southern Methodist Univ.) implant were 35 ± 6% and 32 ± 9%, respectively. It failed to reach statistical significance ($p > 0.05$). The peak pushout force for Endopore (Innova Corp.) and EBM (Southern Methodist Univ.) implants were 198.80 ± 61.29 N and 243.21 ± 69.75 N, respectively. The apparent shear stiffness between bone and implant for the Endopore (Innova Corp.) and EBM (Southern Methodist Univ.) implants were 577.36 ± 129.99 N/mm; and 584.48 ± 146.63 N/mm, respectively. Neither the peak pushout force nor the apparent shear stiffness of the implants was statistically different between the two groups ($p > 0.05$). The results suggest that the implants manufactured by EBM (Southern Methodist Univ.) perform equally well as the commercial implant Endopore (Innova Corp.) in this current animal model.

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